potential roles of these ion channels in regulating proliferation and migration.

Methods: Multiple experimental approaches were employed in this study, including whole-cell patch voltage-clamp, RT-PCR, Western blots, cell proliferation and migration assays, etc.

Results: Several ionic currents were heterogeneously expressed in human cardiac c-kit$^+$ progenitor cells, including a large conductance Ca^{2+}-activated K^+ current (BKCa) in most (93%) of cells, an inwardly-rectifying K^+ current (I_{Kir}) in 87% of cells, a transient outward K^+ current (I_{to}) in 39% of cells, a voltage-gated tetrodotoxin-sensitive Na^+ currents ($I_{Na,TTX}$) in 76% of cells. Molecular identities of these ionic currents were determined with RT-PCR and Western blot analysis. KCa.1.1 (for BKCa), Kir2.1 (for I_{Kir}), Kv4.2, Kv4.3 (for I_{to}), NaV1.2, NaV1.3, NaV1.6, NaV1.7 (for $I_{Na.TTX}$) were expressed in human cardiac progenitor cells. Inhibition of BK_{Ca} with paxilline, I_{to} with 4-aminopyridine, but not $I_{Na.TTX}$ with TTX and I_{Kir} with Ba^{2+}, decreased cell proliferation. Silencing of KCa.1.1, Kv4.2 or Kv4.3, but not Kir2.1, with siRNA targeting corresponding channels reduced proliferation. Inhibition of KCa1.1 or Kv4.2 or Kv4.3 channels accumulated cells at G0/G1 phase. Interestingly, down regulation of KCa1.1, Kv4.2 or Kv4.3 channels decreased, while of Kir2.1 channels increased migration in human c-kit$^+$ progenitor cells.

Conclusions: These results demonstrate for the first time that multiple ion channels are expressed in human cardiac c-kit$^+$ cells. KCa1.1, Kv4.2, and Kv4.3 channels, but not Na^+ channels and Kir 2.1 channels, participate in regulating proliferation. KCa1.1, Kv4.2 or Kv4.3 channels promote, while Kir2.1 channels reduce cell migration in human cardiac c-kit$^+$ progenitor cells.

P17

CHRONIC INTERMITTENT HYPOXIA INDUCES OXIDATIVE STRESS AND INFLAMMATION VIA ANGIOTENSIN II RECEPTOR 1 IN RAT LIVER

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Chronic intermittent hypoxia (IH) associated with obstructive sleep apnea (OSA) is characterized by repetitive cycles of hypoxia and reoxygenation, leading to excessive production of reactive oxygen species and oxidative stress in tissues and organs. However the mechanistic effects of chronic IH on the liver are not clear at present. We hypothesized that renin-angiotensin system (RAS) plays a role in the IH-induced oxidative stress and tissue inflammation in the rat liver.

Adult Sprague-Dawley rats were exposed to air (normoxic (Nx) control) or IH treatment (with inspired oxygen fraction in the normobaric chamber cyclic between 5-21% ± 0.5% per min, 8 hours per day) for 14 days. Rats were fed with an angiotensin II type 1 (AT1) receptors blocker telmisartan (10mg/kg body weight), or vehicle daily before the IH treatment. Hepatic expression levels of pro-inflammatory cytokines TNF-α, IL-6, and IL-1β were detected with ELISA assay; serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were examined for liver injury; also the level of oxidative stress with malondialdehyde (MDA) in the liver.

Our results showed that the protein expression of IL-6, TNF-α and IL-1β were significantly higher in the hypoxic group than that of the Nx control and telmisartan-treated hypoxic (TIH) groups, suggesting that inhibition of the binding of angiotensin II to AT1 receptors attenuates IH-induced tissue inflammation in the rat liver. In addition, the MDA level was significantly elevated in the hypoxic group but was normalized by the telmisartan treatment. Furthermore, the serum ALT to AST ratio was increased significantly in the hypoxic group when compared to the Nx and TIH groups.

In conclusion, blockade of the AT1 receptor mitigates oxidative stress, tissue inflammation and cellular injury in the liver of rats exposed to chronic IH mimicking a severe OSA condition, thus supporting a pathogenic role of RAS in the IH-induced hepatic injury.

P18

NADPH OXIDASE UPREGULATED BY AT1 RECEPTOR MEDIATES CHRONIC INTERMITTENT HYPOXIA-INDUCED OXIDATIVE STRESS AND INFLAMMATION IN RAT ADRENAL MEDULLA

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